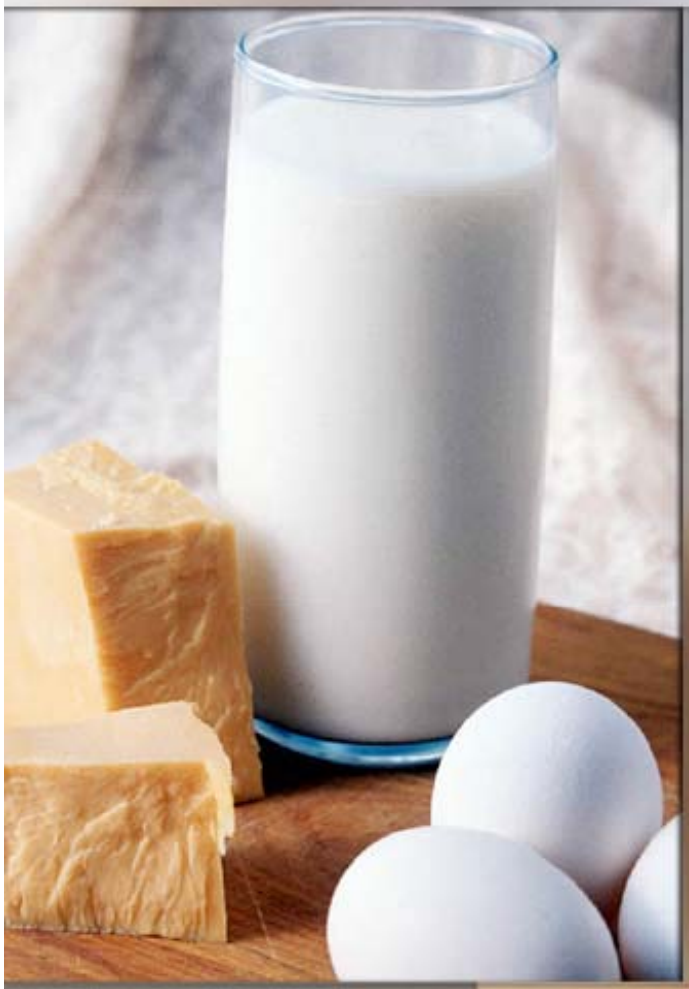

Reaching Decisions on "Tolerable Level of Risks" – Observations of FDA's Approaches for Foods

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Decisions

- Each day industry and government agencies must make decisions about the safety of foods and food products
  - The public health and economic well-being consequences of bad decisions can be substantial
  - Not deciding is not an option
- During the past 15 years there has been a tremendous effort both in the United States and throughout the international food safety community to make decisions that are public health based, risk based, transparent, and consistent
- Understanding concepts such a “tolerable levels of risk” have been integral to this evolution in thought

Presentations

- Introduction
- FDA regulatory framework
- FDA as a risk management agency
- Appropriate level of protection
- Setting “thresholds”
- Risk management metrics
- Concluding remarks

Tolerable Level of Risk

Basic Concepts

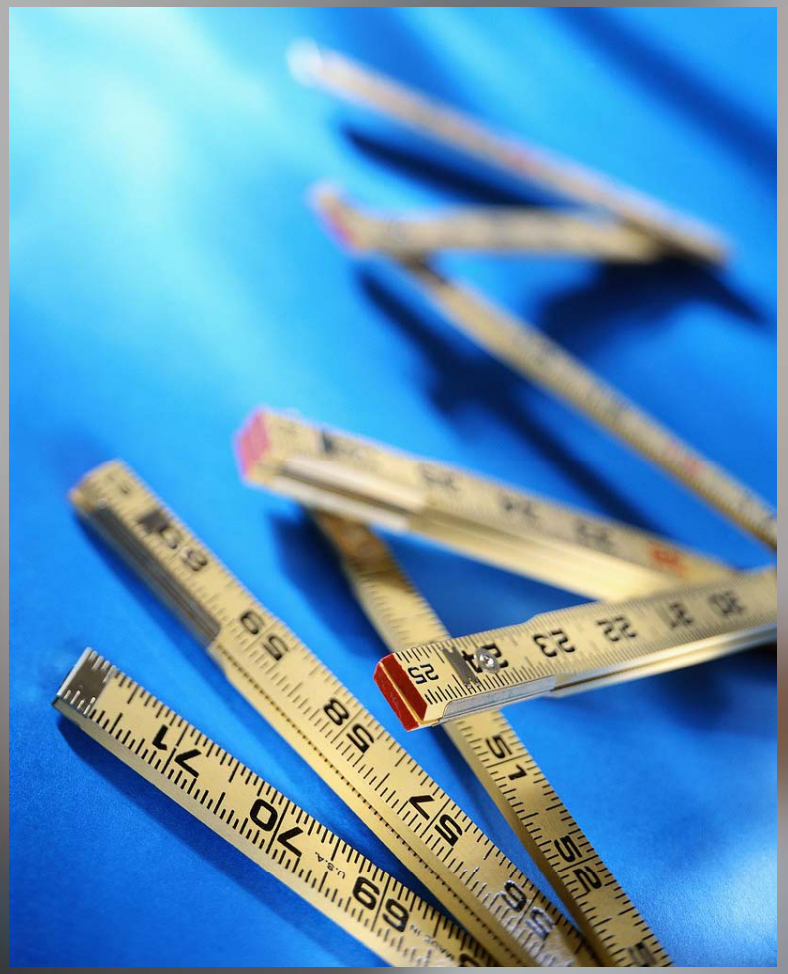
- **Basic Assumption:**
  - **The degree of "regulatory control" should be proportional to the risk to public health**

Basic Concepts

- **Managing Uncertainty Is an Integral Part of Decisions**
  - Use “safety margins” to offset uncertainty
  - Extent of precaution should be proportional to uncertainty and risk (probability + severity)
  - Qualitative or quantitative consideration of uncertainty is integral to our decisions (e.g., 100-fold uncertainty factors used with safety assessments)

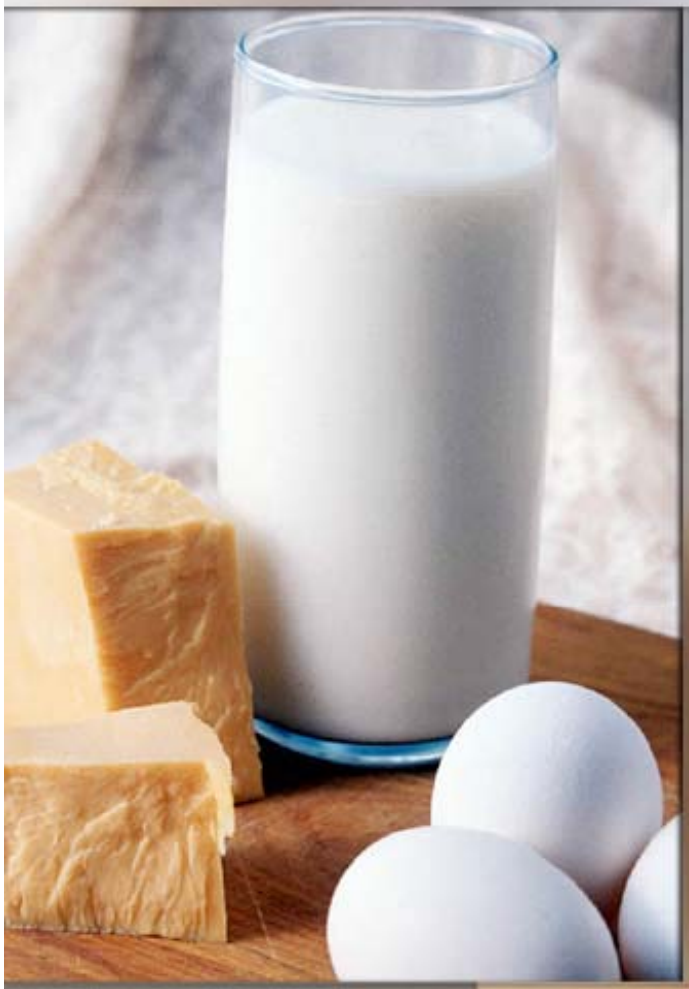
Basic Concepts

- You cannot regulate what you cannot measure



Basic Concepts

- For the purposes of this talk, will assume that the following are synonomous:
  - Tolerable level of risk
  - Acceptable level of risk
  - Appropriate level of protection
- Articulate the level of stringency we expect from food safety systems



FDA Regulatory Framework

FDA Food Safety Policy

- Food safety policies are an integration of science and law

Food and Drug Administration

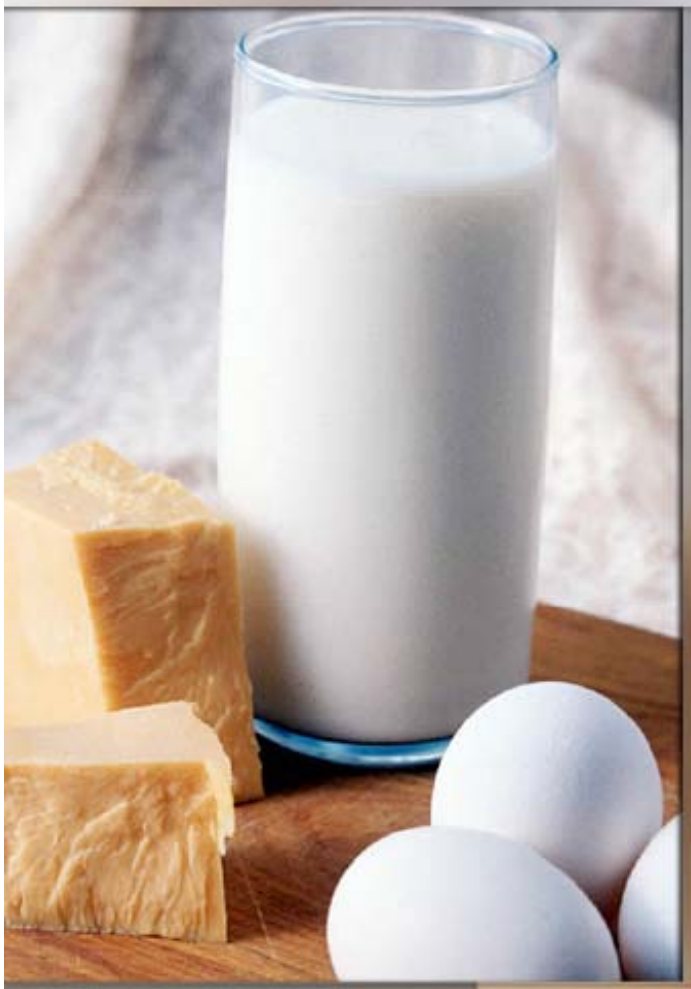
- Charged with enforcing the Federal Food, Drug, and Cosmetic Act (21 USC 301 *et seq.*) (FFDCA)

Food and Drug Administration

- FFDCA establishes:
  - Conditions that lead to a food being considered
    - Adulterated ***
    - Misbranded
  - Pre-market approval requirements for
    - Food Additives
    - New dietary supplements
    - Infant formula
  - Requirements for nutrition labeling
  - Registration of food manufacturers and prior notice requirements

Federal Food, Drug, and Cosmetic Act

- **SEC. 402. [21 U.S.C. 342] A food shall be deemed to be adulterated— (a)**
  - **(1) If it bears or contains any poisonous or deleterious substance which may render it injurious to health; but in case the substance is not an added substance such food shall not be considered adulterated under this clause if the quantity of such substance in such food does not ordinarily render it injurious to health;**
  - **(3) if it consists in whole or in part of any filthy, putrid or decomposed substance, or if it is otherwise unfit for food;**
  - **(4) if it has been prepared, packed, or held under insanitary conditions whereby it may have become contaminated with filth, or whereby it may have been rendered injurious to health;**
  - **Other sections**



FDA as a Risk Management Agency

Food Safety Decisions

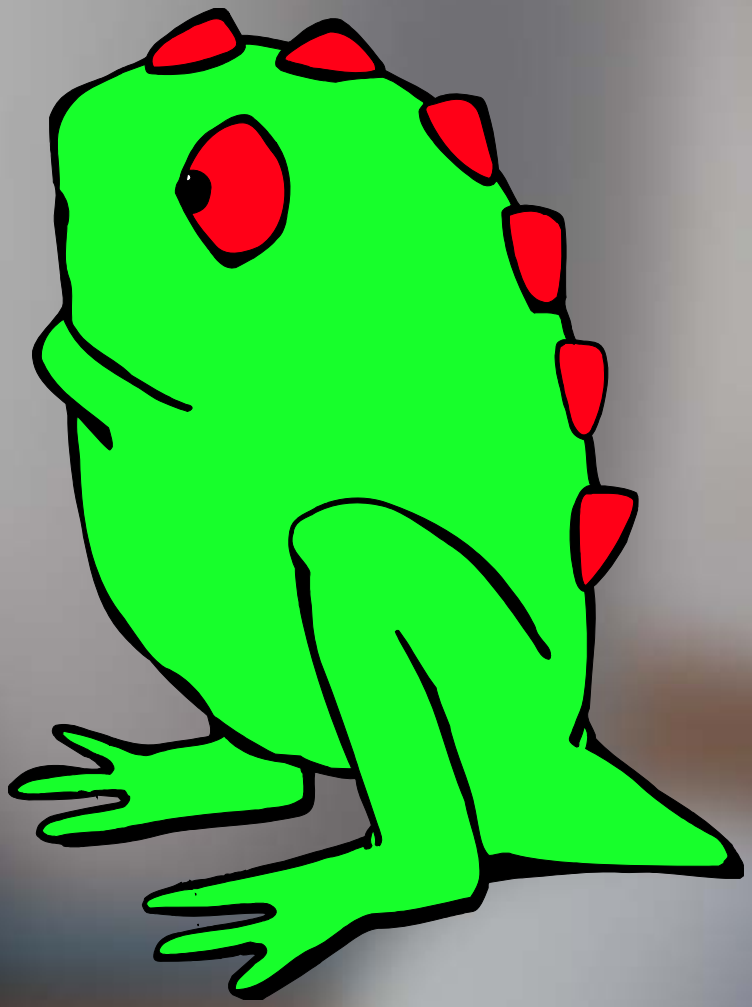
- While we have always managed risks, FDA reached a critical cusp in its ability to take decisions
  - Provide transparent public health based, risk based decision
  - Optimize competing risks
  - Deal effectively with the diversity of the population and the marketplace
  - Deal with the international interdependence of the marketplace
- Accelerated by advances in risk-based decision-making tools

Evolving Food Control Frameworks

- Traditionally, the degree of control of food safety concerns other than food additives have been based on the concept of achieving control "As Low As Reasonably Achievable" (ALARA)

Evolving Food Control Frameworks

- ALARA-based systems are often controversial
- "Reasonable," like beauty, is in the eyes of the beholder



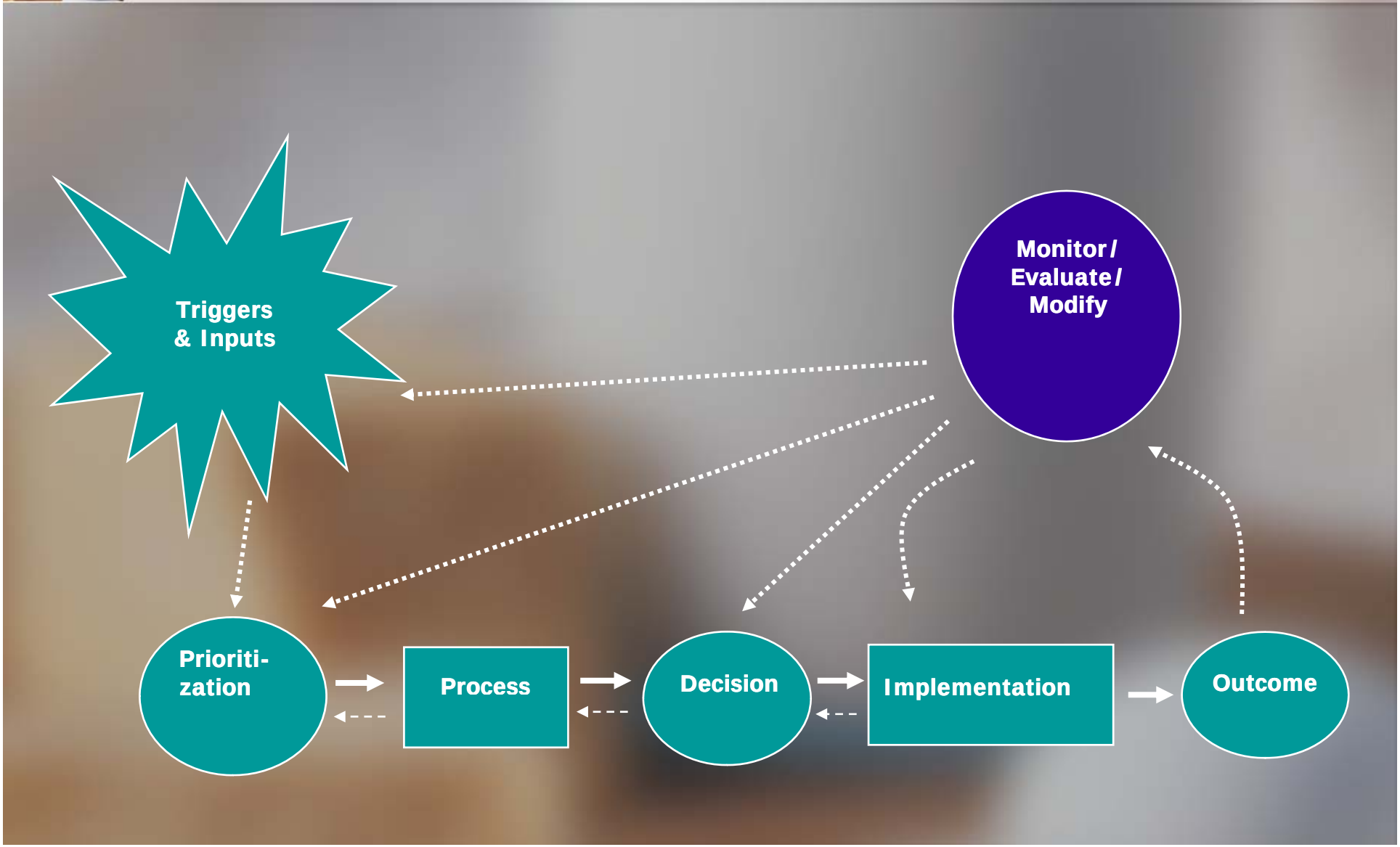
Evolving Food Control Frameworks

- **Disputes arise when:**
  - an industry is very heterogeneous in relation to technological capabilities or resources
  - the technological capabilities or approaches of two countries differ greatly
  - there is no clear cut means of controlling a hazard
  - Expectations of a country's consumers and/or its public health community differ from industry's or an exporting country

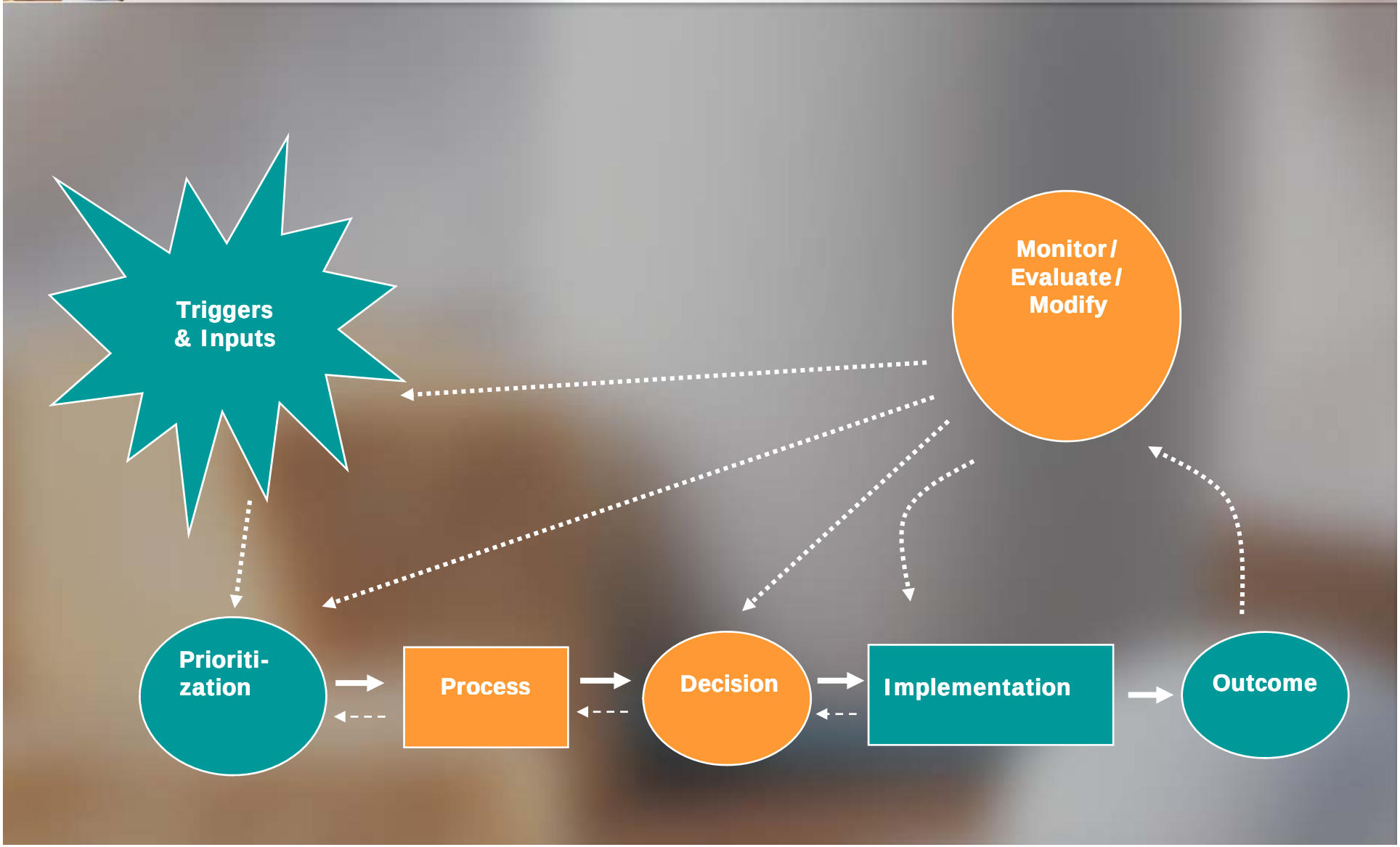
Evolving Food Control Frameworks

- Have seen an evolution in how we consider and manage food safety hazards within a risk management framework
  - 1850 – 1960: "Father Knows Best" System
  - 1950 – 1990: Early HACCP
  - 1980 – Present: Benchmarked HACCP
  - 1995 – Present: Public health goal based risk management

FDA/CFSAN Risk Management Framework



FDA/CFSAN Risk Management Framework



Drivers

- **Science**
  - Sensitive analytical methods
  - Attribution increasingly possible
  - New technologies allow observation of more subtle biological effects
  - Dealing with the diversity of individuals
  - Advances in the evaluation of risk
    - Risk assessment methodologies
    - Evidence-based approaches
    - Connecting actions and standards to public health outcomes

Drivers

- **Public health**
  - Emergence of global public health issues
    - Movement of people and products
    - Obesity, toxic contaminants, infectious diseases
  - Global coordination of public health surveillance, prevention, and treatment efforts
  - Emergence of public health and consumer advocates
  - Impact of global communications
  - Complexity of the food supply

Drivers

- **Regulatory**
  - Embracing risk management principles
    - Science based while considering societal concerns
    - Transparency
    - Consistency / Proportionality
    - Outcome-based
      - Maximize public health protection
      - Minimize disruption of trade
  - Foster innovation
  - Reduced budgets for regulatory agencies; need to prioritize hazards / risks
  - Emergence of WTO
  - Harmonization of international standards

World Trade Organization (WTO)

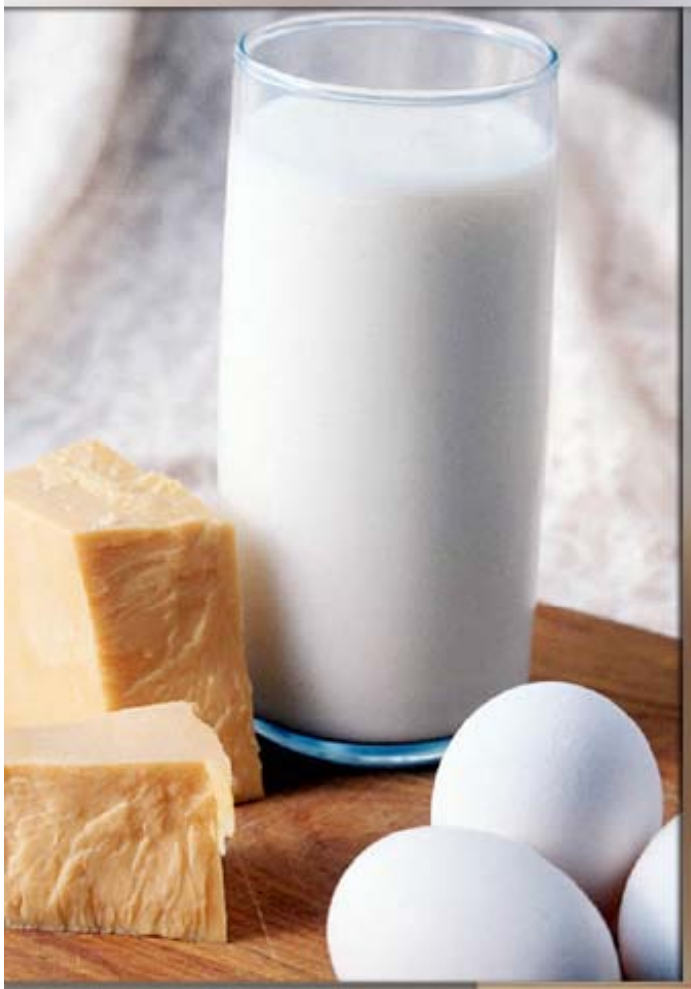
- For international trade in food, two of the most important agreements are the “Sanitary and Phytosanitary (SPS) Agreement (SPS)” and the “Technical Barriers to Trade (TBT) Agreement”
- Introduced the concept of “Appropriate Level of Protection”

Appropriate Level of Protection

- Concept introduced by WTO SPS agreement
  - "Level of protection deemed appropriate by the member (country) establishing a sanitary or phytosanitary measure to protect human, animal or plant life or health within a territory"
- Has strongly influenced countries into thinking about "tolerable level of risk"

Appropriate Level of Protection

- ALOP is not a determination of "how many bodies" we are willing to accept
  - Always striving to find ways to reduce the impact on public health
- ALOP measures what is achievable today before "costs" to society become too great
  - Not just economic cost!!!
- Will implicitly or explicitly take into account uncertainty



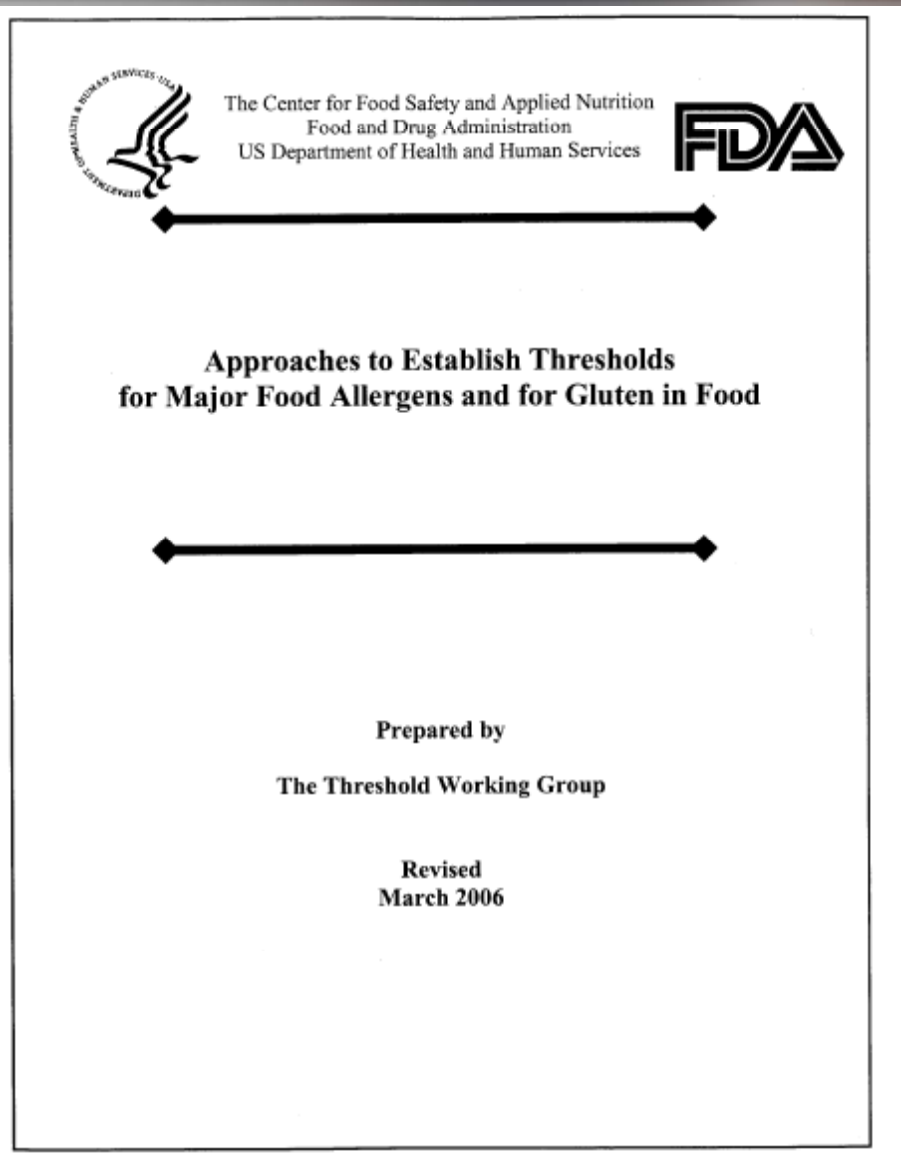
Setting Thresholds

Thresholds

- Implicitly or explicitly a decision has to be made about “tolerable risk”
- Done by setting a threshold
  - Methodologically-based
  - Biologically-based
    - Safety assessment
    - Risk assessment
    - If not biologically based threshold can be determined, can establish a tolerable level of risk based threshold (“threshold of regulatory concern”)
  - Statutorily-based

Thresholds

- Good discussion of the application of the concept of thresholds to a food safety issue
- Developed in response to FALCPA



The Center for Food Safety and Applied Nutrition
Food and Drug Administration
US Department of Health and Human Services

FDA

Approaches to Establish Thresholds for Major Food Allergens and for Gluten in Food

Prepared by

The Threshold Working Group

Revised
March 2006

Approaches To Establish Thresholds For Food Allergens

- Analytical Methods-Based
- Safety Assessment-Based
- Risk Assessment-Based
- Statutorily Derived

Analytical Methods-based Approach

- Based on sensitivity of methods
- Used when validated methods are available
- Not directly linked to public health outcomes

Safety Assessment-Based Approach

- LOAELs or NOAELs from clinical data
- Uncertainty factors based on data gaps

Risk Assessment-Based Approach

- Response distributions from clinical data
- Exposure distributions from dietary history data
- Derive quantitative estimates of risk (probability of adverse effect and uncertainty)
- Most technically rigorous approach

Statutorily Derived Approach

- Based on “highly refined oil” language in FALCPA
- Link between thresholds and public health unclear

Factors Affecting Thresholds

- Setting a "tolerable level of risk" is both a scientific and a societal consideration
- Both aspects must be considered in establishing one

Picking a Level

- The risk level set is based to a great extent on whether a case would be supported in court based on the interpretation of the FFDCA
- Interpretation of those phrases are a dependent combination of
  - Science
  - Policy
  - Case law
  - Past practices / consistency

Picking a Level

- Stringency for a specific hazard / food pair is dependent on
  - Severity of hazard
  - Public perception of the hazard
  - Ability of the consumer to control the hazard
  - Population affected
  - Extent of consumption
  - Avoidability
  - Potential for control
  - Alternative foods
  - Etc

Picking a Risk Level

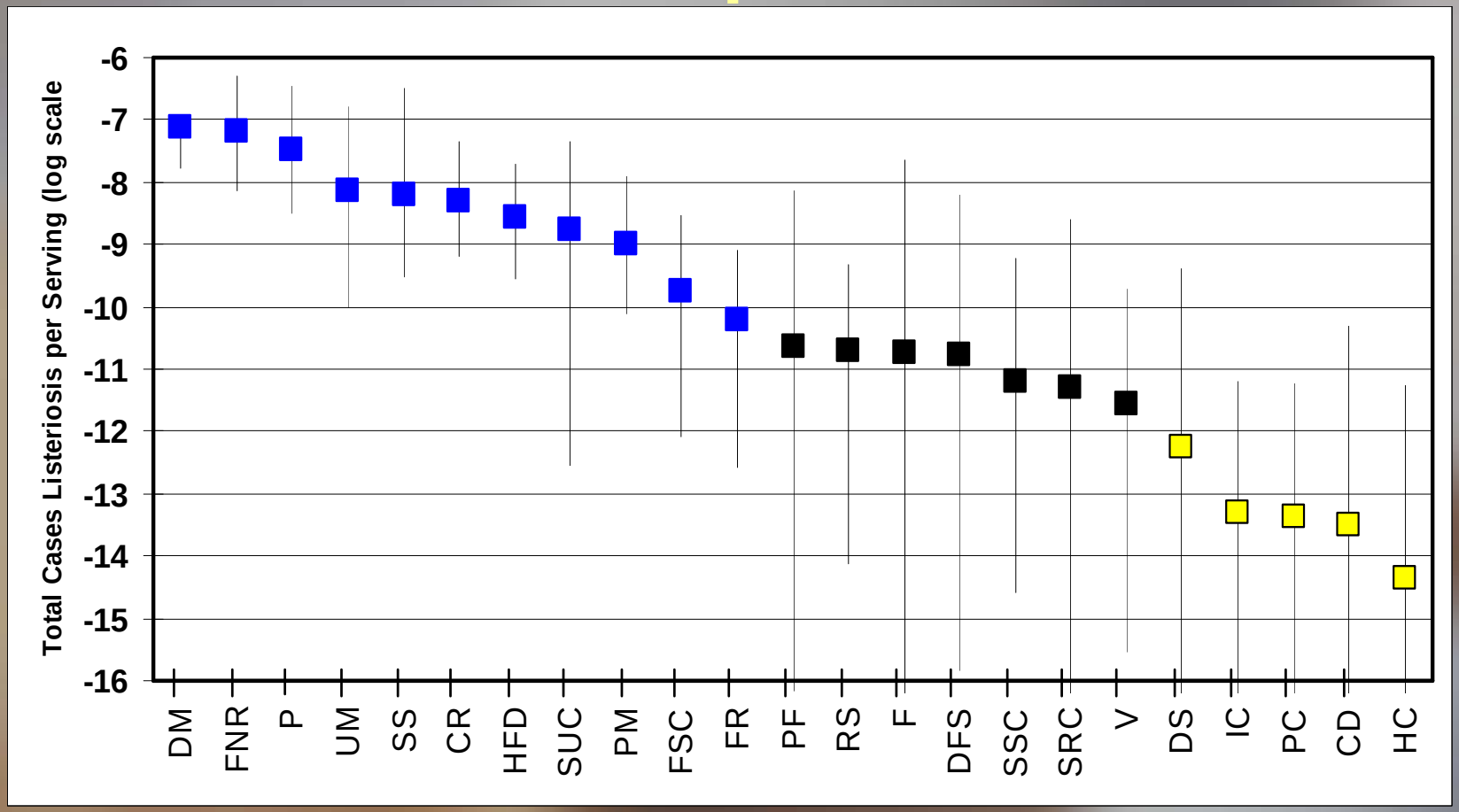
- Dependent on the nature of hazard and its effect – ability to establish a biologically based threshold
  - Acute toxic chemicals: Definable thresholds?
  - Toxigenic bacteria and fungi: Definable thresholds?
  - Indirect food additives: Threshold of regulatory concern (impact above background)
- With chemical contaminants there is a long history of using risk assessments and safety assessments within legal framework
  - Chemical contaminants
  - Food additives

Picking a Level

- Where the ability to establish a biological threshold is unclear, a risk assessment helps reach an informed decision about the extent of food safety control that can be reasonably expected
  - Carcinogens
  - Infectious agents
  - Allergens???

Listeria monocytogenes

Estimated Cases of Listeriosis per Serving Total Population



Listeria monocytogenes

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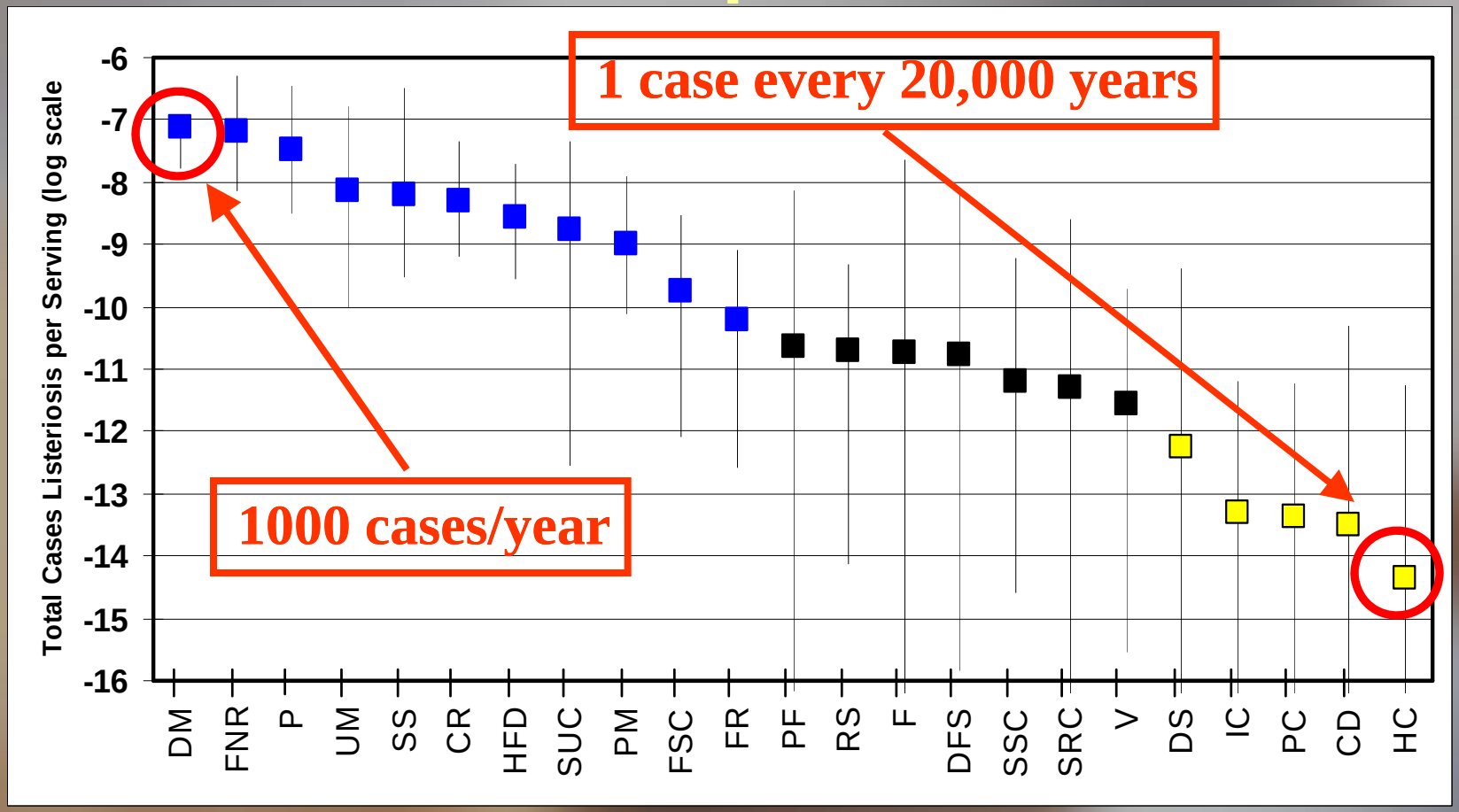


Picking a Level

- In instances where a threshold cannot be established and the hazard is unavoidable, a regulatory threshold is established
  - Directly:
    - Tolerance (section 406), regulatory limit (section 409) - **Seldom done**
    - Action level – **Regulatory discretion**
    - Compliance Policy Guide – **Regulatory discretion**
  - Indirectly:
    - Through establishment of an official method/sampling plan that indicates how the regulatory agency will look for the hazard

Picking a Level

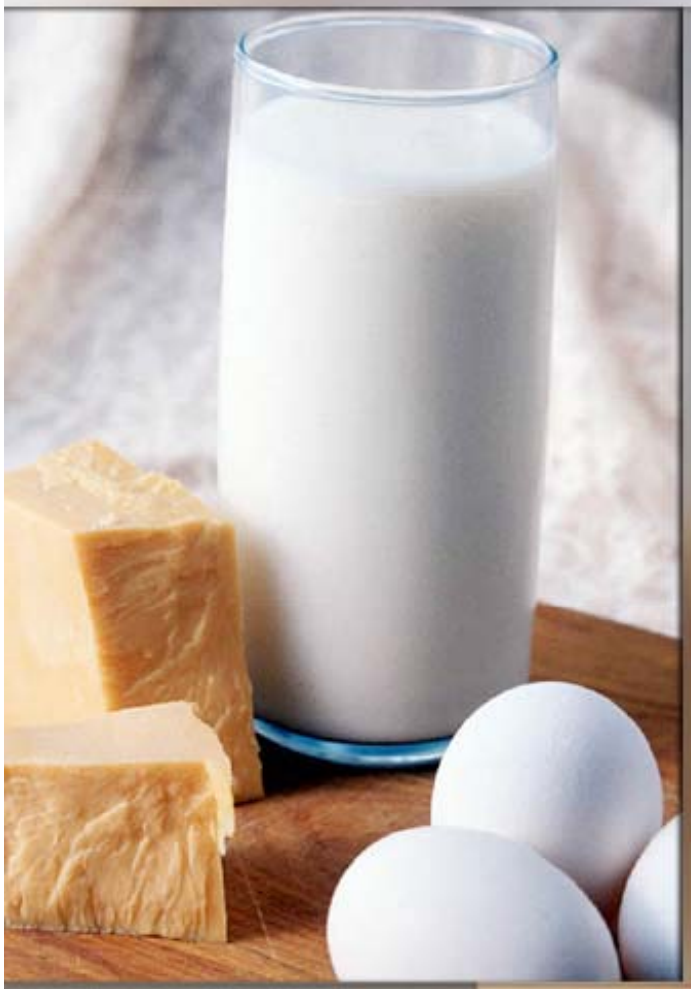
- If requires a new regulation, must be established by a process required by Administrative Procedures Act (5 USC 553)(APA)
  - Advance Notice of Proposed Rulemaking (Optional)
  - Proposed Regulation
  - Final Regulation
- Assures consideration of science, transparency, and stakeholder involvement
- Critically important that the scientific community is involved

Picking a Level

- Developing new regulations (and to a lesser extent category #1 guidance) may have additional requirements such as
  - Economic analysis
  - Risk Assessment
  - Information Quality Act
  - OMB Risk Assessment Guideline
  - Paperwork Reduction Act
  - Environmental Impact
- Involvement of all stakeholders in decision making is critical

Picking a Level

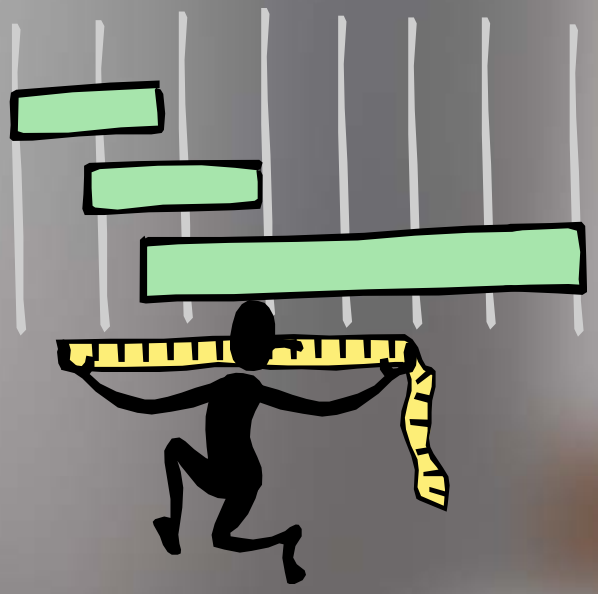
- Concept of a “zero tolerance” expresses an attitude but has no meaning scientifically
- As soon as one attempts to verify a “zero tolerance,” they must specify a sampling protocol, i.e., either a methods-based threshold or an implied biologically based threshold



Measuring Compliance to a "Tolerable Level of Risk"

Risk Analysis Metrics

- Integral components to a risk analysis approach to food safety is being able to relate the stringency of a food control system to its intended public health outcome and then verify that it is being achieved



Risk Management Metrics

- Quantitative microbial risk assessments deal in distributions and probabilities
- Conversely, the law is a binary system; safe or not safe
- Establishing the stringency of a food control system is meaningless unless it can be verified
- Can consider variability in establishing decision criteria but ultimately a consistent "yes or no" decision must be reached
- Need a means to convert a risk distribution to a yes/no decision

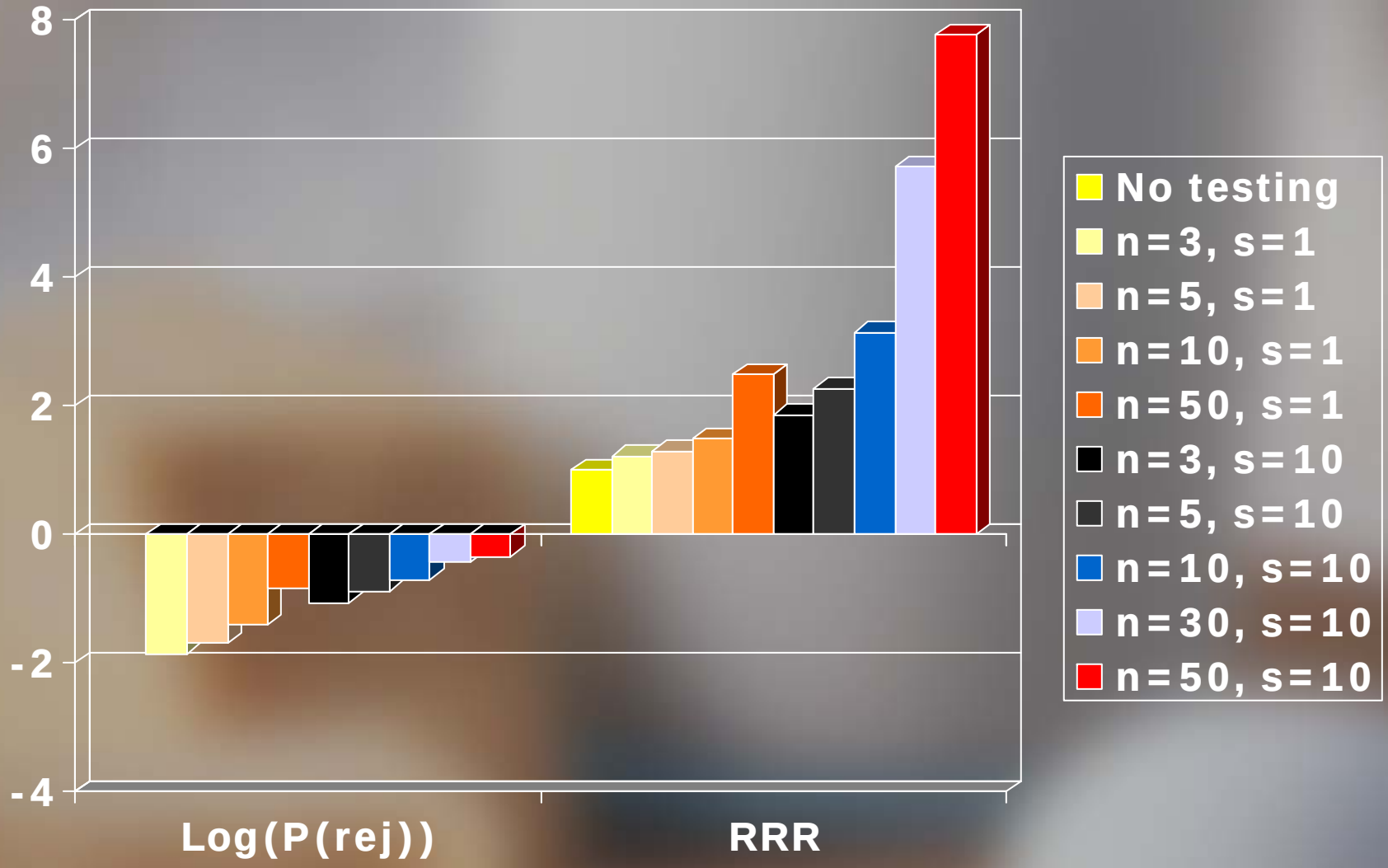
Codex Alimentarius – *Enterobacter sakazakii*

- Draft Code of Hygienic Practice for Powdered Formulae for Infants and Young Children
  - Annex I: Microbiological Criteria for Powdered Infant Formula, Formula for Special Medical, and Human Milk Fortifiers

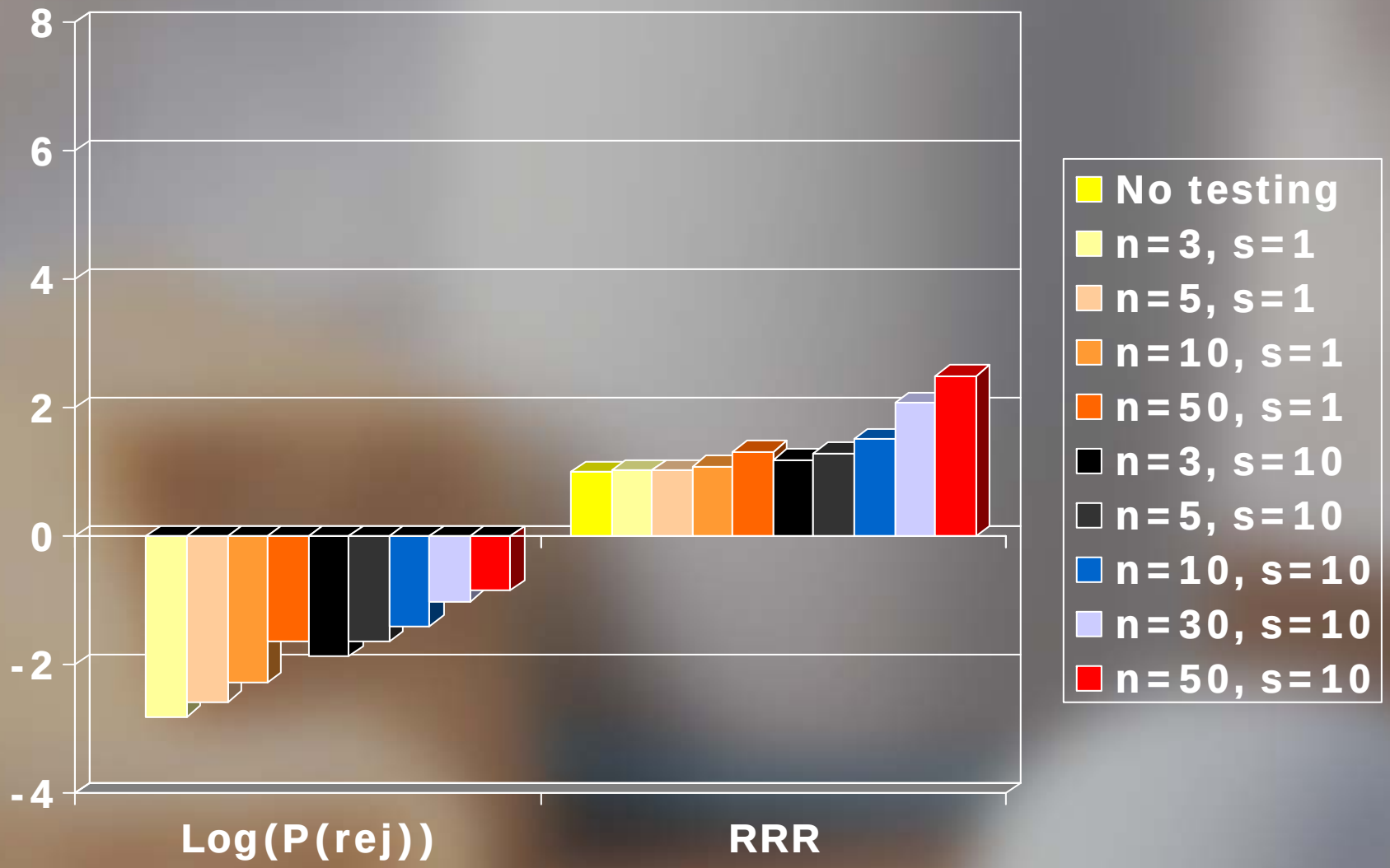
Powdered Infant Formula

- *Enterobacter sakazakii*
  - Causes septicemia and menningitis in neoates and infants
  - Two risk assessments performed by FAO/WHO (JEMRA)
  - One examined the effect of lot-by-lot sampling on relative risk reduction
  - http://www.fao.org/ag/agn/agns/jemra_riskassessment_enterobacter_en.asp

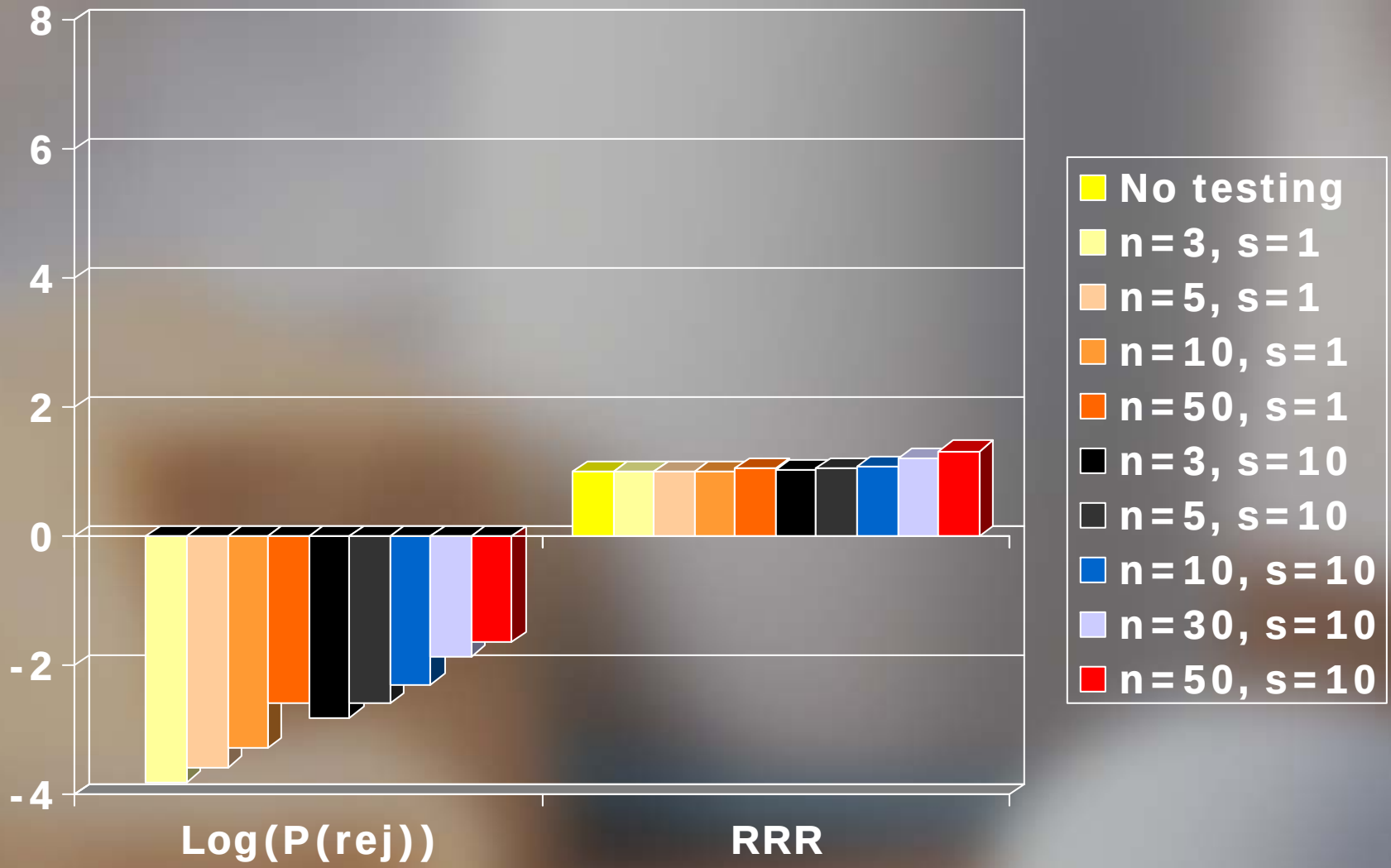
Mean Contamination: 10^{-3} CFU/g



Mean Contamination: 10^{-4} CFU/g



Mean Contamination: 10^{-5} CFU/g



Concluding Remarks

- The FDA (and the other food safety regulatory) have a long history of working with concepts related to “tolerable levels of risk”
- The new tools in risk assessment, along with the new risk management requirements are making this concept much more transparent